Palliative treatment of advanced oesophageal cancer

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Abstract. *The poor prognosis of patients with advanced oesophageal cancer is proof of its ability to spread. Locoregional spread is often discontinuous, i.e. distant regional lymph nodes may be invaded even when local nodes are free of tumour. In patients with potentially curable cancer, we advocate subtotal oesophagectomy pioneered in the UK by McKeown on the grounds that generous proximal clearance gives the best chance of clearing satellite nodules in the submucosal lymphatics and gives the best postoperative function with the least tendency for gastro-oesophageal reflux. Patients who have an incurable disease should not be submitted to needlessly aggressive treatment that simply prolongs the process of dying, so the role of palliative resection is debatable. Major changes to the management of patients with oesophageal cancer have been made in the 1990s, including increased sub-specialization, better staging by spiral CT and EUS and greater use of adjuvant radiotherapy and chemotherapy. Whether or not these changes have made any difference to clinical outcome is as yet unknown. Most of the patients with unresectable cancer die with severe dysphagia and a poor quality of life. The aim of this article is to evaluate all palliative methods how to relieve dysphagia, which limits the quality of the patient's life, and the creation of an algorithm of decisions in the management of patients with cancer of the oesophagus.*

Key words: *cancer of the oesophagus, a self-expanding stent, radiotherapy, chemotherapy, bougienage, laser treatment*

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Zhrnutie. *Prognóza pacientov s pokročilým karcinómom pažeráka je zlá. Lokoregionálne šírenie nádoru nie je kontinuálne, tzn. môžu byť postihnuté vzdialené lymfatické uzliny napriek tomu, že lymfatické uzliny v okolí primárneho nádoru môžu byť bez postihnutia.*

U pacientov s potencionálne kurabilným ochorením (na základe stagingu) v súčasnosti na našom pracovisku vykonávame subtotálnu ezofagektómiu technikou podľa McKeowna so snahou o odstránenie submukóznych lymfatických ciev v čo najväčšom rozsahu proximálnym smerom a snahou o minimalizovanie možného pooperačného gastroezofageálneho refluxu. U pacientov s pokročilým ochorením, u ktorých je možná len paliatívna liečba je našou snahou obmedziť prílišnú agresivitu liečby, ktorá by teoreticky len predlžovala proces umierania. Paliatívna resekcia pažeráka ako jedna z metód paliatívnej liečby je na našom pracovisku indikovaná v presne vymedzených štádiách ochorenia s cieľom odstrániť primárny nádor, čo považujeme za základ úspechu v boji s karcinómom pažeráka. Väčšina pacientov však už pri prvom kontakte s lekárom prichádza s neresekovateľným karcinómom resp. resekcia pažeráka nie je indikovaná vzhľadom k štádiu ochorenia a celkovému stavu pacienta. 90-te roky sú spojené s veľkými zmenami v taktike liečby karcinómu pažeráka, sú spojené so subšpecializáciou

lekárov, presnejším určením stagingu pomocou endosonografie a špirálového CT a širším využitím adjuvantnej rádioterapie a chemoterapie. Či tieto zmeny výraznejšie ovplyvnia kvalitu života resp. prežívanie pacientov nie je zatiaľ jednoznačne dokázané. Cieľom tohto článku je zhodnotenie základných paliatívnych metód liečby karcinómu pažeráka s prihliadnutím na kvalitu života pacienta. Vypracovanie algoritmu liečby pacienta v pokročilom štádiu tohto ochorenia.

Kľúčové slová: *karcinóm pažeráka, endoprotézy, rádioterapia, chemoterapia, bužiovanie, laserová liečba*

Cancer of the oesophagus was already described in China 2000 years ago as Ye Ge, which means dysphagia and belching. But only since the end of the 19th century has there been a change in medical opinion about the disease and attempts have been made to actively help patients with oesophageal cancer.

Histologically, approximately 95 % of oesophageal cancers worldwide are squamous cell carcinomas. Between January 1999 and December 2003, 108 patients with non-resectable malignant oesophageal stenosis were examined in our Department of Surgery, University Hospital, Bratislava. There were 95 % male and 5 % female. In 84 % the oesophageal stricture was due to a squamous carcinoma and in 14 % to an adenocarcinoma. Malignant tumours of the oesophagus other than typical epidermoid carcinoma are listed in Table 1. Some trials have pooled squamous cell carcinoma with adenocarcinoma, which may be unwise because of different aetiology, different responses to treatment and different outcomes after treatment (86).

Table 1
Malignant tumours of the oesophagus

PRIMARY TUMOURS
A. Malignant epithelial tumours
1. Squamous cell carcinoma - variants (verrucous, polypoid)
2. Adenocarcinoma - variants ("ordinaire", cylindroma, muco-epidermoid, adenoacanthoma)
3. Oat Cell Carcinoma
4. Melanoma
B. Mesenchymal tumours
1. Leiomyosarcoma
2. Rhabdomyosarcoma
3. Fibrosarcoma
4. Chondrosarcoma
II. METASTATIC TUMOURS TO THE OESOPHAGUS

Adenocarcinomas constitute 2.5 - 8 % of primary oesophageal cancers, although this frequency is increasing dramatically in the United States at a rate surpassing that of any other cancer (8,42). They occur most commonly in the distal third of the oesophagus and may have one of three origins:

1. malignant degeneration of metaplastic columnar epithelium - Barrett's mucosa. Barrett's oesophagus is transformation of the stratified squamous epithelium of the distal oesophagus into columnar type epithelium with specialized intestinal metaplasia. If there is only gastric, or more rarely, pancreatic type epithelium found in the oesophagus, there is no increased cancer risk. If there is intestinal metaplasia present, then there is an increased risk of adenocarcinoma. Patients with Barrett's metaplasia are 40 times more likely to develop adenocarcinoma than the general population (10, 74).
2. heterotopic islands of columnar epithelium
3. oesophageal submucosal glands

Adenocarcinomas of the oesophagus have a better prognosis than squamous cell cancers (71). There are three different subsisting classification systems for carcinomas in the gastro-oesophageal junction: Liverpool, Munich and ICD-O. Overall, adenocarcinomas of the lower oesophagus and adenocarcinomas involving the gastro-oesophageal junction have similar clinico-epidemiological, pathological and molecular features no matter which classification is used (25).

Oat cell carcinoma demonstrates neurosecretory granules on electron microscopy and survival beyond 1 year is unusual (68).

Adenoid cystic carcinoma (cylindroma) - typically occurs as a middle-third oesophageal tumour, metastasizes widely and is associated with a median survival of only 9 months (29).

Melanoma - generally occurring as a large polypoid mass, with an average survival of 13 months (68).

Mesenchymal tumours - typically polypoid tumours

in the distal two thirds, huge size (more than 10 cm) and 5-year survival 2 - 6 % (88).

Despite dramatic technical advances over the last 50 years, certain controversies remain over the effectiveness of therapy. They range from the pessimistic view, that the entire treatment is only palliative, to the radical one that total oesophagectomy in selected cases may provide a curative outcome.

CONTROVERSIES IN THE TREATMENT OF OESOPHAGEAL CANCER

In contrast to the incidence of gastric cancer, which is decreasing worldwide, the incidence of oesophageal cancer is increasing at an alarming rate in the Western world, primarily because of an increase in the rate of adenocarcinoma of the distal oesophagus (22). Despite marked advances in surgical therapy for oesophageal, oesophago-gastric, and gastric cancers, the overall prognosis of patients with these diseases has not improved markedly during the past few decades because, in the Western world, these tumours continue to be diagnosed at an advanced stage in most affected patients (77) and the 5-year survival has remained worryingly poor at less than 10 % (14,29,30).

Problem 1. Discovery of the disease at the late, inoperable stage

It seems like a paradox, but the palliative treatment of oesophageal cancer still lingers somewhat in the background, although statistically, the number of patients in whom radical surgery is feasible, is only 39 % (25). As long as early detection of oesophageal cancer does not become routine, palliative therapy will continue to prevail over the effective cure of the disease. Early detection in the future would involve the utilization of routine cytological screening for squamous cell oesophageal cancer and good surveillance at patients with Barrett's oesophagus. Great hopes have been placed also into genetic markers.

Problem 2. Determination of a generally acceptable, accurate preoperative staging system

Stage-directed management strategies have become essential, because of the increased number of treatment modalities available. In addition, accurate staging enhances the quality of clinical trials, see Table 2.

Table 2
Tumour-Node-Metastasis (TNM) staging system for oesophageal carcinoma
Adapted from the American Joint Committee on Cancer (4) and Sobin et al. (75).

PRIMARY TUMOUR (T)
Tx primary tumour cannot be assessed
T0 no evidence of primary tumour (e.g. after treatment)
Tis carcinoma in situ
T1 tumour invades lamina propria or submucosa
T2 tumour invades muscularis propria
T3 tumour invades adventitia
T4 tumour invades adjacent structures
REGIONAL LYMPH NODES (N)
Nx regional nodes cannot be assessed
N0 no regional node metastasis
N1 regional node metastasis
DISTANT METASTASIS (M)
Mx presence of distant metastasis cannot be assessed
M0 no distant metastasis
M1 distant metastasis

The use of endoscopic ultrasound (EUS) in oesophageal cancer staging has become routine in dedicated centres. Conventional EUS could successfully traverse 43 % of tumours, the mini-probe with a diameter of 2.7 mm was successful in all cases. The overall accuracy of conventional EUS plus wire-guided system was 62 % compared with 86.8 % for the mini-probe. This was significant only for T-stage. For N-stage comparable accuracy rates were obtained (55).

The identification of involved coeliac lymph nodes is important in the stage-directed treatment of oesophageal cancer, because their involvement signifies stage M1a/b (stage IV) disease (78). The accuracy of computed tomography (CT) scans and conventional EUS is less than 70 % (76). Criteria of size greater than 1 cm, round, homogeneous echo pattern, and sharp borders were used to define positive nodes (12). Further improvement is expected if more refined criteria are used. With the widespread use of neoadjuvant therapy, post-treatment re-staging has assumed more importance, but accuracy with current methods is not optimal in this setting (49).

According to stages, oesophageal cancer is divided into 4 main groups that determine operability and potential curability. Stages 0, 1 and 2 are considered potentially curable, but one has to emphasize that in stage IIB the stage of the tumour is T1/T2 and not T3, see Table 3. As soon as the tumour is placed in stage III, it indicates that the cancer has reached size T3 with involvement of the lymphatics. It is rarely resectable to affect a cure. Stage IV with distant metastases is usually incurable and inoperable.

Table 3
Stage grouping for oesophageal carcinoma
Adapted from the American Joint Committee on Cancer (4).

Stage 0	T is	N 0	M 0
Stage I	T 1	N 0	M 0
Stage IIA	T 2	N 0	M 0
	T 3	N 0	M 0
Stage IIB	T 1	N 1	M 0
	T 2	N 1	M 0
Stage III	T 3	N 1	M 0
	T 4	any N	M 0
Stage IV	any T	any N	M 1

Problem 3. Technique and strategy of the surgical procedure

It can be summarily stated that there are 2 main views concerning the treatment of oesophageal cancer. One states that patient survival depends on the stage of the disease in which it is diagnosed. The other view is convinced that the technique and tactics of the surgical procedure can influence the preoperative staging and hence the survival of the patient with oesophageal cancer.

By combining these views, one can opine that the treatment of oesophageal cancer is still searching for its proper place and algorithm. However, it seems clear that only a multidisciplinary approach and the understanding of all available therapeutic modalities can be successful, and the physician - in most cases the surgeon - can decide about the most appropriate way to treat his/her patient.

METHODS OF PALLIATIVE TREATMENT OF OESOPHAGEAL CANCER

If a patient's lesion is considered incurable on preoperative or intra-operative evaluation, palliative therapy is provided only if the patient has symptoms that can be palliated. Not all symptoms can be. Dysphagia above grade III (see Table 4), vomiting from obstruction, bleeding from the tumour, and pain from ulceration are indications for palliation (11).

Table 4
Functional grades of dysphagia in patients with oesophageal cancer
Adapted from Sugahara et al. (80).

Grade	Definition
I	Eating normally
II	Requires liquids with meals
III	Able to take semi-solids but unable to take any solid food
IV	Able to take liquids only
V	Unable to take liquids but able to swallow saliva
VI	Unable to swallow saliva

Every treatment plan is individual and depends on the stage of the tumour, on the symptoms, age and morbidity, as well as on the needs and desires of the patient.

I. Surgical resection and removal of the tumour

In oesophageal cancer the distinction between palliative and curative surgical therapy is more difficult than in other neoplasia. Often only during the operation it is possible to decide whether surgery will be palliative or may result in a complete cure.

In our department, we perform subtotal oesophagectomy in oesophageal cancer, with the removal of all accompanying lymph nodes. Surgery may be considered palliative or curative, depending on the intraoperative findings and the results of histological examination. The most significant prognostic factors in patients with oesophageal cancer undergoing oesophago-gastrectomy are the completeness of resection (R-category), ratio of metastatic nodes to total nodes resected, and the presence of vascular invasion (89).

Staging, typing and grading of the tumour, which will ultimately determine the survival of the patient, are more important than the type of surgery.

Surgical techniques:

A. Blunt transmediastinal dissection (without thoracotomy)
B. Transthoracic resection

Table 5.
Methods of palliative treatment of oesophageal cancer

METHODS OF PALLIATIVE TREATMENT	
A. PALLIATIVE RESECTION	1. BLUNT TRANS-MEDIASTINAL DISSECTION
	2. TRANS-THORACIC RESECTION
B. BYPASS METHOD	3. EXTRACORPOREAL SYSTEM INTERCONNECTED WITH HOSE
	4. INTERCONNECTION: STOMACH, JEJUNUM, COLON
C. ENDOPROSTHESES	5. SURGICAL INTERVENTION
	6. ENDOSCOPIC INTERVENTION
	7. FLUOROSCOPIC INTERVENTION
D. LASER TREATMENT	8. NEODYMIUM - YAG
	9. PHOTOSENSITIVE MEDIUMS
E. THERMAL TREATMENT	10. ARGON PLASMA COAGULATION
F. ALCOHOL INJECTIONS	11. 96 - 98% ALCOHOL
G. BOUGIENAGE	12. CONVENTIONAL
	13. THERMO-BOUGIENAGE
	14. MICROWAVE-BOUGIENAGE
H. ANATROPHIC STOMIA	15. SURGERY: GASTRO- OR JEJUNOSTOMY
	16. PERCUTANEOUS ENDOSCOPIC GASTROSTOMY
	17. FLUOROSCOPIC GASTROSTOMY OR JEJUNOSTOMY
I. RADIOTHERAPY	18. PERCUTANEOUSLY, ^{60}CO, ELEMENTARY PARTICLE ACCELERATOR
	19. INTRACAVITARY
J. CHEMOTHERAPY	20. SYSTEMIC
	21. LOCAL
K. SYMPTOMATIC TREATMENT	22. TREATMENT OF PAIN
	23. ALIMENTATION
	24. THERAPY OF PULMONARY COMPLICATIONS
	25. TREATMENT OF BLEEDING COMPLICATIONS
	26. ORAL SCENT TREATMENT
	27. DETECTION OF THE QUALITY OF LIFE
	28. SOCIAL ISSUES

II. Surgical (non-resection) bypass procedures

Since the introduction of intubation and laser techniques, bypass procedures are losing in importance. It is, however, necessary to be familiar with them because, despite appropriate preoperative staging, conditions may develop, when during surgery the tumour proves to be irremovable. Then, if the thoracic cage had already been opened, palliative bypass procedures may become appropriate alternatives.

Esophago-gastrostomy:
A. Lortat-Jacob
B. Frangenheim-Gavriliu

It can be said in summary that oesophageal bypass techniques are demanding procedures, taxing to the patient as much as radical resections, while the tumour remains in situ. Results of these procedures are not favourable for the following reasons: the tumour continues to grow, relief of dysphagia is not better than that achieved by modern methods of recanalization, lethality is quoted at 20 - 40 % and last but not least the mean survival time is only 5 months (87).

Meunier et al. (56) performed bypass procedure in 32 patients who had either persistent dysphagia after radiochemotherapy or a tracheo-oesophageal fistula. The lethality rate was over 30 %.

III. Intubation by endoprosthesis

Intubation of the oesophagus as a palliative treatment of dysphagia in malignant oesophageal obstruction has been known for over 100 years (5,19). In 1959, Celestin described palliation of oesophageal cancer by means of a plastic endoprosthesis introduced by laparotomy (13). This thought was developed by Dotter in 1969 (26). Atkinson in the seventies, introduced plastic prostheses by endoscopy and was able to somewhat reduce complications (3). The internal diameter of such stents was small (10 - 12 mm) and caused difficulties in the majority of patients once they started consuming regular food. The number of complications remained high (up to 39 %) particularly as a consequence of oesophageal perforation during the introduction of the stent. Lethality in connection with the endoscopic procedure was between 2 - 16 % (82). At present, the plastic stents have been replaced by a new series of metallic self-expandable stents that are more secure and easier to insert (3,6,20,36,47,67-70). These metallic stents, following the necessary improvement in medico-technical equipment, have been in clinical use mainly in vascular surgery, where they found their primary usefulness in the mid eighties (62,73). At present, stents have been routinely used in biliary strictures (17), in urinary and respiratory obstructions (68), and they have been introduced also in the area of the upper and lower gastrointestinal tract (63).

The first report of endoscopic insertion of an expandable spiral metallic stent was published by Frimberger in 1983 (33). Currently, as prior methods were fraught with relatively high morbidity and lethality, the stent treatment of inoperable oesophageal strictures has been fully accepted as the method of choice in strictly defined cases.

The advantage of this method is the ease of introduction in uncomplicated cases under conscious sedation. The stent, in a compressed form, is introduced by mouth, after release its internal lumen extends and becomes flexible, hence it is more effective and the patients are able to consume normal food. The success of insertion is high. Stent treatment is currently considered the most appropriate method of recanalization, bringing the patient the best subjective and objective improvement in swallowing (1,16,23,24,34,47,48,76,84,86).

Indications for insertion of self-expandable stents in cancer of the oesophagus and cardia:

- Inoperable tumours of the oesophagus and cardia
- Conditions following resection of the oesophagus and stomach with recurrence of cancer in the anastomosis with proof of inoperability and generalized spread of the disease
- Malignant oesophago-respiratory fistulae (incidence in the literature is quoted at 5 %), under the provision that coated stents are used
- Malignant strictures of the oesophagus caused by external pressure. These are tumours of the mediastinum, centrally located bronchogenic cancer and lymphadenopathy in other malignant diseases

Due to new knowledge and technological advances, stenting in malignant oesophageal obstructions and refractory benign strictures is constantly evolving. New anti-reflux stents, anti-migration stents with internal plastic coating and new retrievable stents have been developed. The majority of patients (75 - 90 %) can enjoy normal food and have reduced dysphagia following stent insertion.

It was originally thought that stenting in malignant strictures would be a one-step procedure. However, as patient survival increases, recurrence of stenosis occurs in up to 60 % and often another intervention becomes necessary. Patient survival may be further increased by the use of adjuvant chemotherapy or endoluminal brachytherapy before or after stenting but this may cause additional complications. More studies are needed in this area.

The initial cost of the expandable metallic stent is high. But the overall expense is definitely lower, when compared with other palliative methods that frequently need repeated sessions and prolonged hospitalization. In patients with advanced oesophageal malignancy, the determining factor for any particular use of palliation often remains the availability of a given method and/or the experience with it. Larger comparative studies of the variety of metallic stents may demonstrate which stent has the lowest complication rate. It is understood that any stent should be inserted only after a thorough multidisciplinary evaluation of the patient and the appropriate staging of the tumour.

IV. Laser therapy

For the sake of completeness, it is important to mention another choice in the palliative treatment of oesophageal cancer - laser evaporation. This method

uses a contact or focused Nd:YAG laser (see below). Due to its many disadvantages laser evaporation therapy generally is no longer in use.

The disadvantages are:

- The need for repeated sessions
- Length of procedure
- Frequent recurrences of dysphagia
- High cost and low cost-effectiveness in comparison with other methods

Endoluminal laser therapy

This treatment utilizes a neodymium/yttrium-aluminium-garnet (Nd:YAG) laser and is probably the most widely used method of first line therapy. It is used for the ablation of obstructing tumours especially in patients with short tumorous stenosis or with large endoluminal tumorous mass. Palliation is achieved in up to 80 % of patients (31,32,58). However, it is necessary to repeat the laser sessions every 4 - 8 weeks and palliation is not as good as with the use of metallic stents (1). There was no difference in the improvement score for dysphagia among laser therapy, plastic stents or metallic stents in the studies of Gevers et al. (34) or Konigsrainer et al. (49).

Photodynamic laser therapy

Photodynamic therapy is currently used in the treatment of various malignancies, including oesophageal cancer. To improve the transfer of light energy onto the oesophageal mucosa, special balloons are employed. The pressure of the balloon may cause a decrease in flow and oxygenation of the mucosa and thus a reduced effect of the photodynamic therapy (61). Intravenously administered porphyrin-photosensitive materials are selectively concentrated in the malignant tissue, which is then destroyed by the application of the laser beam. Palliation of dysphagia is similar or better than with laser therapy alone in 90 % of cases (51). One should not overlook the decreased incidence of perforations in this type of therapy because there is no need for prior dilatations. The limiting factor is the high cost of equipment and the shallow depth of light penetration into the tumour requiring repeated applications. The side effects of the administration of photosensitive materials are frequent and the patients have to avoid direct sunlight. These methods are valuable primarily in those cases, where insertion of a stent may be a problem, such as in the region of the upper oesophagus, at the gastro-oesophageal junction, and following radiation and chemotherapy (39,51,53,54).

V. Argon plasma coagulator or bipolar electrocoagulation

These methods enable the direct coagulation of the tumorous mass under endoscopic control. The coagulation with argon plasma enables energy transmission to tissue through ionized gas (argon) with high-frequency at a wave length of 488 and 514 nm, which are absorbed by haemoglobin and melanin with a penetration depth of no more than 1 mm. Limitations of this technique are the absence of tissue vaporization and limited tissue deep necrosis, which could be extended to the first 3 mm. Tumorous stenosis of the oesophagus requires prior dilatation, so the coagulation probe can reach the tumour located distally. Effective palliation is achieved in over 80 % of patients (40). The number of complications is similar to those in laser therapy, particularly due to potential perforations that occur, depending on various studies, in up to 8 %. Byrne et al. (9) suggested that the risk of perforation could be due to a coagulation excess or the probe coming into contact with the oesophageal wall, as a result of an unexpected movement of the patient.

The equipment needed for this type of technique is relatively inexpensive but repeated sessions are necessary in more than 26 % of patients (66,85).

VI. Alcohol injections

Ninety-seven percent alcohol injected into the tumorous tissue under direct endoscopic control causes necrosis of the neoplasm. Prior dilatation is usually needed and according to one study, it was impossible to get beyond the tumorous stenosis in up to 18 % of cases (14). However, complications are less frequent than in other thermal ablative methods, despite a good early response to therapy the frequency of recurrences is relatively high. In medical literature, experience with this method is limited (59). These ablative techniques can be used in the treatment of endoluminal tumour overgrowth or epithelial hyperplasia in patients with recurrent dysphagia following stent insertion.

VII. Bougienage

This treatment can be performed on an outpatient basis. The diameter of the bougie is gradually increa-

sed either in one session or gradually in several. The disadvantage of this method is the need for repeated sessions after a certain time, if dysphagia recurs due to tumour growth. The procedure requires considerable experience and care of the operator.

The introduction of the balloon dilation catheter brought a radical change. Balloon dilators were originally used for the distension of vascular stenoses in the pelvic and femoral circulation and later also in other areas of the cardiovascular system. Currently the use of balloon catheters became common place in endoscopic practice. Increased safety is achieved by placement of the balloon into the stricture under X-ray control and on a guide wire, i.e. not blindly as in some types of bougies. This way the risk of perforation practically diminishes. In addition, dilatational forces act radially in the area of the tumour stenosis, which reduces the risk of fissure formation. In order to improve dysphagia, the oesophagus has to be dilated to a diameter of 15 - 20 mm. Unfortunately, the effect is short-lived.

VIII. Feeding stomies

Modern mini-invasive surgery, with its effort to return a patient to home care early, has dramatically changed the view on the nutrition of a surgical patient. The increasing popularity of enteral feeding in various clinical states can be attributed mostly to two factors:

- Development of a simple and low-risk procedure for placement of tubes in the gastrointestinal tract, particularly percutaneous endoscopic gastrostomies and jejunostomies
- Availability of a wide variety of commercial enteral feeding formulas with diverse nutrient components. Today there are more than 100 types of commercial solutions for enteral feeding available

Access to the stomach can be achieved by percutaneous endoscopic gastrostomy (PEG), open gastrostomy or laparoscopic technique. PEG was first submitted in 1980 by Ponsky and Gauderer. Before this time only temporary gastrostomies have been carried out on all oncological patients. These gastrostomies were placed via a midline laparotomy incision and double purse string technique.

IX. Radiation therapy

In oesophageal cancer there are no randomized studies comparing surgical treatment with radiotherapy. The British Medical Research Council attempted such a clinical trial but it was terminated prematurely (27). At present, patients are referred to radiotherapy alone, if preoperative examination reveals inoperable disease or any other condition preventing radical surgery. Three to 27 % of patients treated by radiation alone survived 2 years, 0 - 20 % had a 5-year survival (57).

In the absence of randomized studies that would assess survival and local or regional changes, as well as morbidity and mortality, it is difficult to compare palliative surgery with radiation therapy alone. In patients undergoing curative radiotherapy alone, a 5-day scheme/week is recommended with a dose of 1.8 - 2.0 Gy daily without interruption to a total dose of 60 - 65 Gy. In many patients dysphagia improves significantly, although in some it may worsen temporarily during therapy. The duration of improvement following treatment is variable. In about half of the patients the improvement lasts at least for 2 months, less than 15 % experience improvement of dysphagia for more than 12 months. A dose of 45 - 50 Gy is recommended for palliative treatment (60,74). Five studies comparing adjuvant radiotherapy (using a total dose of between 20 - 40 Gy) with surgical resection alone have failed to document any advantage of one over the other as far as survival is concerned (37,46,64,80).

Brachytherapy

Although external beam radiotherapy has its firm place in the management of oesophageal cancer, its therapeutic potential is extremely low. In 1980, Earlam and Cunha-Melo (28) reported a one-year survival in 18 %, two-year survival in 8 % and 5-year in 6 % of patients with oesophageal cancer. Although temporary relief of dysphagia can be achieved, there is a relatively rapid local recurrence of the disease in 80 %. In order to improve these dismal results, attention was turned in the eighties, to brachytherapy. It was not a new method, Knox in 1915 had already placed radium-filled bougies into the oesophagus of patients with oesophageal cancer with fair results. The disadvantage of this method was the high risk of uncontrolled radiation, both the patient and the medical staff were exposed to. A renewed interest in this method came about in the eighties with new radioactive materials, such as cesium^{137}, cobalt^{60} and iridium^{192} and after the introduction of the "automatic afterload" technique in the management of cancer of

the uterine cervix, which helped to improve the safety of application. The initial success can be ascribed also to the actual dilatation needed for the endoscopic examination and the correct marking of the proximal and distal (aboral) margins of the stenosis. If there is a satisfactory therapeutic response, brachytherapy is repeated if dysphagia recurs. The effect of brachytherapy in adenocarcinoma of the oesophagus was almost as favourable as in spinocellular carcinoma, which happens rarely with external radiotherapy. Side effects, such as oesophagitis, mild epigastric pain, nausea and diarrhoea, were also rare.

Brachytherapy provides a more delicate treatment modality than external beam radiotherapy. Better therapeutic results were achieved by its combination with chemotherapeutic agents such as 5-fluorouracil, methotrexate, bleomycin, adriamycin and/or cisplatin. Today a combination of brachytherapy with chemotherapeutic agents is contraindicated due to risk of oesophageal fistulas. Brachytherapy has no lethality, side effects are minimal and hospitalization short. Dysphagia improves immediately because of mechanical dilatation of malignant stenosis with applicator but therapeutical effect only appears after 4 - 8 weeks. Patient survival is extended. Its disadvantage is the need for repeated treatment sessions because of recurrent dysphagia (44).

X. Chemotherapy

A randomized trial in the USA was conducted in the second half of the nineties (46). It compared the adjuvant administration of cisplatin and 5-fluorouracil in 3 cycles and subsequently in 2 cycles after surgical resection with surgery alone. Preliminary results report that only one third of patients received all 3 scheduled cycles of chemotherapy and 20 % suffered from significant hepatotoxicity. Evaluating the survival in the compared groups, the addition of chemotherapy did not offer any advantage in resectability, in the relapse-free interval or in the overall length of survival.

In a Scandinavian randomized prospective study published in 1992, Hatlevoll et al. (38) administered cisplatin and bleomycin as adjuvant chemotherapy (cisplatin 20 mg/m^2, bleomycin 10 mg/m^2 both on days 1 - 5 and then on days 15 - 19) before radical radiotherapy to patients with localized inoperable oesophageal cancer (35 Gy at 1.75 fractions and then subsequently 28 Gy after 3 weeks). The study failed to document any prolongation of survival, on the contrary toxicity was significant.

Recently, several clinical studies using docetaxel and irinotecan were published with promising results (35,43,45,52).

Definitive chemotherapy and radiotherapy (chemoradiation)

At present chemoradiation has better outcome in local control of the tumour and overall length of patient survival than radiation therapy alone (2,18,41). The results were as good as prior results with surgical therapy alone. A comparison between definitive chemoradiotherapy, with that of adjuvant chemoradiation with subsequent surgery has not yet been made (65).

To summarize:

a) Pathologic complete response is the best predictor of the length of survival.
b) 5-flurouracil either in a short-duration or continuous infusion remains the basis of combination chemotherapy.
c) Novel agents for chemotherapy (docetaxel, irinotecan) are available for advanced, recurrent or metastatic disease.
d) Radiation therapy has to be administered in standard fractional doses of 1.8 - 2.0 Gy without interruption in the overall schedule (79).
e) Only after the availability of results of large randomized prospective studies will it be possible to define the optimal steps of a multi-modal therapy and the need for individual features of this therapy.

CONCLUSION

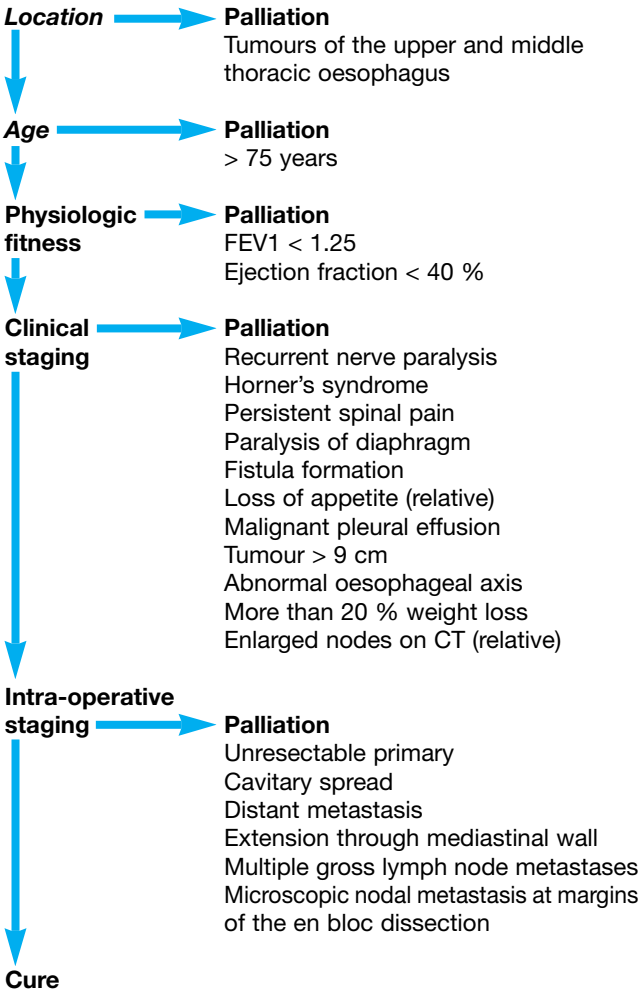
1) Radiotherapy and chemotherapy have limited effects and the results of therapy occur relatively late. In radiotherapy the effect only appears after 4 - 8 weeks and up to 44 % of patients continue to experience dysphagia even after 16 weeks.
2) In chemotherapy the results appear only after about 9 weeks and up to 50 % of patients continue to have dysphagia.
3) Dilatation in oesophageal cancer is an unsuitable method because of the high risk of perforation and short duration of effect.
4) Laser treatment is demonstrably less advantageous than stenting. It is less effective, there is a shorter duration of improvement and it needs to be repeated. Re-treatment with laser therapy is

necessary in 100 % of cases in comparison to 13 % in coated stents.

5) Bypass surgery has a lethality of up to 30 % and requires long-term hospitalization.
6) Rigid plastic endoprostheses carry a complication rate of up to 36 % and successful insertion occurs in 30 - 80 %.
7) The insertion of metallic stents is successful in 80 - 90 % of cases, complications occur in 25 % and lethality is 0 - 6 %. Because of a high risk of dislocation, stent insertion is contraindicated if the diameter of the oesophagus exceeds 15 mm. However, in the absence of major dysphagia stenting may not be necessary.

Carcinoma of the oesophagus has an aura of pessimism among physicians, resulting in an attitude that cure is not possible. At first, we make the selection of patients for cure or palliation. If a patient's lesion is considered incurable on preoperative or intra-operative evaluation, palliative therapy is provided only if the patient has symptoms that can be palliated. There is only one aim of palliation, see Figure 1. It is to improve the quality of life for the limited span of life left to the patient (7). The mean survival in these patients is only 4 - 6 months, whatever therapy is carried out. The most devastating symptom is dysphagia. A simple oesophageal resection and reconstruction with an oesophago-gastrostomy offers the best palliation.

Figure 1
Algorithm of decisions in the management of patients with cancer of the oesophagus and cardia
Adapted from DeMeester et al. (21).



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